

Appl. No. 09/124,485
Proposed Amdt. Dated October 15, 2003 in response to Office Action Of June 2, 2003

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REMARKS/ARGUMENT

Claims 38-43 and 45-47 are under prosecution in this case. Claims 38 and 41 have been amended for improved clarity. No new matter has been added in this Amendment. The detailed discussion of the cited prior art can be found in the previous Responses filed in this case.

Claim Rejection under 35 U.S.C. §112:

Claim 41 is rejected under 35 U.S.C. §112, second paragraph, based on the recitation of "nitric oxide effect". Without acquiescing to this aspect of the rejection, the term alleged to be indefinite in claim 41 has been deleted.

Claim Rejections under 35 U.S.C. §103:

Claims 38-43, and 46-47 are rejected under 35 U.S.C. §103(a) as allegedly unpatentable over Kremsner *et al.* or Anstey *et al.* in view of Green *et al.* Applicants respectfully traverse this rejection.

The invention is a method for preventing or treating an infection by a *Plasmodium* species in a non-rodent mammal by administering an agent that increases nitric oxide levels.

Kremsner *et al.* reported that high plasma levels of nitrogen oxides are associated with severe malaria from screening 3 groups of malarial patients, from uncomplicated to severe. Anstey *et al.* reported that the plasma NO_x levels were inversely related to malarial disease severity with levels lowest in fatal cerebral malaria.

The findings of Kremsner and Anstey are exactly the opposite. Both Kremsner and Anstey studies were published in the same year, 1996. This is a typical example of how confusing this field had been regarding the role of NO in malaria prior to the present invention.

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Contradictory to their findings, Kremsner *et al.* attempted to speculate on the protective role of NO in malaria. The prevailing view at the time was that NO is contra-indicated in malaria. Given this confusing state of the art, those skilled in the art could not have been able to derive any suggestion in either Kremsner *et al.* or Anstey *et al.* to make the invention.

The inventors herein demonstrated for the first time with experimental results in humans that the administration of NO was effective in treating malaria. Up until this invention was made, there have been only correlations and speculations of confusing and contradicting nature. Only with actual efficacy data in humans as illustrated herein, the methods of preventing or treating malaria with an agent that increases NO levels became reality without further doubt.

Green *et al.* describe a generic method of combating infectious disease, e.g., parasite, bacteria or virus by administering NO releasing agents as stated in the Office Action. With the confused messages contained in Kremsner *et al.* (i.e., NO may have a causative role in malaria pathology; increased NO production may be harmful; protective role of NO in malaria etc.) and the prevailing view of the contra-indication of NO in malaria in the art, the teachings of Green *et al.* bear little relevance to the present invention. The confusing and contradictory teachings of Kremsner *et al.* and Anstey *et al.* regarding the role of NO in malaria would not have motivated those skilled in the art to combine the cited references to make the invention. Only with the actual data obtained by the inventors, the present invention of treating or preventing malaria by increasing the level of NO was made possible.

Claim 45 is rejected under 35 U.S.C § 103(a) as allegedly unpatentable over Kremsner *et al.* or Anstey *et al.* as applied to claim 38-43, further in view of Weinberg.

Claim 45 is a dependent claim of claim 38 and further defines the agent that increases NO levels as one selected from the group recited. Accordingly, if claim 38 is not obvious for the reasons described above, claim 45 should not be obvious. It is emphasized that the invention is

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the method of using the agents that increase nitric oxide levels for preventing or treating malaria
not the agents themselves.

In summary, based on the foregoing, the invention as claimed is not *prima facie* obvious over the cited references. Withdrawal of the rejection under 35 U.S.C. §103(a) is respectfully requested.

Conclusion:

Based on the foregoing amendments and arguments, this case is considered to be in condition for allowance and passage to issuance is respectfully requested.

If there are any outstanding issues related to patentability, the courtesy of a telephone interview is requested, and the Examiner is invited to call to arrange a mutually convenient time.

It is believed that this submission does not require the payment of any fees. If this is incorrect, however, please charge any requisite fees to Deposit Account No. 07-1969.

Respectfully submitted,

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